

In re Application of: Dror OFER  
Serial No.: 10/523,131  
Filed: January 21, 2005  
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.  
Group Art Unit: 1631  
Attorney Docket: **35898**  
Confirmation No.: 1264

### **REMARKS**

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-4, 6-25, 29-57, 102, 103, 157-159 and 161-163 are in this Application. Claims 7, 10-13, 16-23, 37-39, 50-53, 57, 102, 103 and 157 have been withdrawn from consideration. Claims 5, 26-28, 58-101, 104-156, 160 and 164-171 have been canceled in a previous response. Claim 1 has been amended herewith.

### **Amendments to the Claims**

#### **35 U.S.C. § 112, Second Paragraph, Rejections**

The Examiner has stated that claims 1-4, 6, 8, 9, 14, 15, 24, 25, 29-36, 40-49, 54-56, 158, 159 and 161-163 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

#### ***Re: Item G***

The Examiner has stated that it is not clear whether the recited point in triangle space has coordinates in such space, and how such coordinates are defined.

The recited point in the triangle space is defined by coordinates, and the coordinates represent the recited triplet of distances and triplet of chemical binding point types which the triangle space defines, as recited in claim 1. Thus, three coordinates represent distances and three coordinates represent binding point types.

In order to clarify this matter, claim 1 has been amended so as to recite:

*“wherein said point in said triangle space is defined by six coordinates, three of said coordinates being for defining the three distances in said triplet of distances, and three of said coordinates being for defining the three binding point types in said triplet of chemical binding point types”*

In re Application of: Dror OFER  
Serial No.: 10/523,131  
Filed: January 21, 2005  
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.  
Group Art Unit: 1631  
Attorney Docket: **35898**  
Confirmation No.: 1264

Applicant therefore believes to have overcome the Examiner's rejection in this respect.

*Re: Item F*

The Examiner has stated that a triangle space seems to be an infinite number of permutations of binding points and distances between them, and it is not clear what constitutes a precisely defined cut-off parameter of 50 % of such space.

Applicant believes that this matter may be more readily understood in view of the abovementioned amendment.

The triangle space indeed comprises an infinite number of points, as each of the coordinates which represent distance (as discussed hereinabove) may assume any of an infinite number of values. However, although the coordinates may assume any of an infinite number of values, the values are within the recited range of 2 to 12 angstrom.

Thus, the triangle space does not have an infinite, unbounded size, wherein the values of the coordinates are limitless. Rather, the triangle space encompasses an infinite number of points within a finite, bounded size of the triangle space.

In this respect, the recited triangle space is similar to a simple 3-dimensional space such as a volume of a container, which also comprises an infinite number of points, with three coordinates (e.g., representing x-, y-, and z-axes) which can assume any of an infinite number of values within defined ranges (e.g., the boundaries of the container).

Applicant submits that there is no difficulty or ambiguity involved in determining what constitutes 50 % of a defined 3-dimensional space such as a volume of a container. Hence, it would be clear to one of skill in the art what constitutes 50 % of a triangle space, because although the triangle space defines an infinite number of possible triplets of distances, the triangle space does not differ in this respect from a defined volume.

In re Application of: Dror OFER  
Serial No.: 10/523,131  
Filed: January 21, 2005  
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.  
Group Art Unit: 1631  
Attorney Docket: **35898**  
Confirmation No.: 1264

Furthermore, the three coordinates which represent binding point types do not represent an infinite number of possibilities. Rather, each of the three coordinates can correspond to any of the six recited binding point types, such that there are 216 ( $6 \times 6 \times 6$ ) possible triplets of binding point types. Hence, there are 216 points in the triangle space for each triplet of distances.

Applicant submits that the existence of a finite and precise number (i.e., 216) of points in triangle space for each triplet of distances does not create any difficulty in determining what constitutes 50 % of the triangle space.

As an example, the coverage of a certain percentage of a triangle space by a triangular configuration can be envisioned, for the sake of simplicity, by considering binding to hypothetical 3-point pharmacophores characterized by binding points B1, B2 and B3, each binding point being selected from one of two possible types of binding points (type X and type Y), and distances D1, D2 and D3, each distance being in a range of 2 to 12 angstrom, while neglecting redundancy of triangles.

Thus, for example, a triangular configuration which hypothetically is capable of binding to any 3-point pharmacophore wherein D1, D2 and D3 are each any distance in a range of 2-6 angstrom (i.e., a range covering 40 % of the possible distances in the range of 2-12 angstrom), and B1, B2 and B3 are each binding point type X (i.e., one of  $2^3 = 8$  possible combinations of binding point types), would cover  $1/8 \times (40\%)^3 = 0.8$  % of triangle space (a higher percentage when redundancy of triangles is taken into account).

In contrast to the simplistic example above, the triangle space recited in claim 1 is more complex (e.g., there are 6 possible types of binding point rather than 2) and the triangular configurations are in general capable of binding only to 3-point pharmacophores with a narrower range of distances. Hence, each configuration will typically cover a smaller percentage of triangle space as compared to the above example. This provides the method of claim 1 with more specificity than would be obtained from the simplistic example above.

In re Application of: Dror OFER  
Serial No.: 10/523,131  
Filed: January 21, 2005  
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.  
Group Art Unit: 1631  
Attorney Docket: **35898**  
Confirmation No.: 1264

Applicant therefore believes to have overcome the Examiner's rejection in this respect.

*Re: Item H*

The Examiner has stated that with respect to the phrase "configuration of binding points capable of chemically binding to each 3-point pharmacophore" that it is unclear how a configuration of binding points can be capable of chemically binding to each pharmacophore of the recited triangle space.

Applicant did not intend that a single configuration of binding points is capable of binding to each pharmacophore. Rather, a single configuration of binding points is capable of binding to certain 3-point pharmacophores. However, the plurality of gauges encompasses many configurations of binding points, such that each 3-point pharmacophore is capable of being bound by some (e.g., at least six), but not all, of the configurations of binding points.

In order to clarify this matter, claim 1 has been amended so as to recite:

*"said plurality of gauges is selected such that for each 3-point pharmacophore corresponding to a point in said portion of triangle space, said plurality of gauges comprises at least six gauges with a substantially rigid triangular configuration of binding points capable of chemically binding to said 3-point pharmacophore"*

Applicant therefore believes to have overcome the Examiner's rejection in this respect.

*Re: Item I*

The Examiner has stated that it is not clear whether the triangular substructure is the same or different from the gauges addressed in the preceding part of the claim, and if they are the same, it is not clear what information, if any, can be obtained by analyzing interactions of compounds (gauges) that are capable of chemically binding to each (i.e., without any specificity) pharmacophore.

In re Application of: Dror OFER  
Serial No.: 10/523,131  
Filed: January 21, 2005  
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.  
Group Art Unit: 1631  
Attorney Docket: 35898  
Confirmation No.: 1264

As discussed hereinabove, the claim has been amended in order to make clear that the gauge molecules are not capable of non-specifically binding to each pharmacophore.

Rather, each gauge molecule comprises at least one configuration of three binding points capable of binding certain 3-point pharmacophores (but not each pharmacophore) and the 3-point pharmacophores are capable of being bound by some (but not all) of the configurations of binding points of the gauge molecules. Hence, the binding of gauge molecules to 3-point pharmacophores is specific (i.e., individual gauge molecules bind only to certain 3-point pharmacophores) and therefore can provide information.

Furthermore, as discussed in the instant application, an individual triangular substructure does not necessarily correspond to an individual gauge molecule, as a gauge molecule may (and in some embodiments usually does) comprise more than one triangular substructure (see for example, Figure 4A as well as from page 33, line 28, to page 34, line 9, of the instant application), and a particular triangular substructure may be present on more than one type of gauge molecule (see for example, page 37, lines 17-19, of the instant application).

Applicant therefore believes to have overcome the Examiner's rejection in this respect.

*Re: Item J*

The Examiner has stated that the information to be analyzed is obtained from an *in vitro* assay of interactions of a set of gauges, but that it is not clear how chemically specific such information would be, that it is not clear where any source of spatial information originates, if all that is known is an *in vitro* interaction with a geometrical substructure, and that is not clear how *in vitro* assays will measure an interaction with a geometrical triangular structures used to describe the compounds used in the assays (for example, it is not clear how functional and binding assays such

In re Application of: Dror OFER  
Serial No.: 10/523,131  
Filed: January 21, 2005  
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.  
Group Art Unit: 1631  
Attorney Docket: **35898**  
Confirmation No.: 1264

as a DNA replication assay can be used to characterize spatially and chemically specific configurations of binding points).

Applicant submits that in view of the considerable guidance provided in the instant application, one of skill in the art would be capable of obtaining chemically and spatially specific information from an *in vitro* assay of interactions of a set of gauges, using a computational model with triangular geometric substructures, as described in the instant application.

By way of example, it is discussed below how spatially specific information may be obtained from results of assays which simply measure whether a gauge has bound to a target or not. Such assay results provide binary information (i.e., binding/no binding) for the gauge. It is to be understood that this merely serves as an example, and assay results may provide other forms of information, as discussed in the instant application.

Such information may be obtained, for example, in a functional binding assay, an effect of a gauge on a function of a target (e.g., activity of a protein target, replication of a DNA target) indicates that the gauge has bound to the target, and moreover, to a region on the target which affects the function of the target.

Assay results for a plurality of gauges provide information as to which gauges bind to a target and which do not. As binary information (i.e., binding/no binding) is obtained for each gauge, and each gauge has a specific structure and chemical properties, the information which may be obtained from analysis of the assay results is chemically specific. The spatial specificity of each gauge (e.g., distances between moieties of the gauge) provides spatial information, and the specific chemical properties of the moieties of each gauge provide chemical information.

By considering the sets of three binding points which are present in gauges which bind the target and/or gauges which don't bind, it is possible to identify triangular substructures (representing sets of gauge binding points) which match the

In re Application of: Dror OFER  
Serial No.: 10/523,131  
Filed: January 21, 2005  
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.  
Group Art Unit: 1631  
Attorney Docket: **35898**  
Confirmation No.: 1264

target and/or substructures which don't match the target (see for example, pages 38-40, Section 6.1, of the instant application).

As discussed hereinabove, triangular substructures (and the sets of three binding points which they represent) comprise a structure which is chemically specific (e.g., with respect to binding point types) and spatially specific (e.g., with respect to distances between binding points) and are suitable for binding only to certain matching 3-point pharmacophores in a target. Hence, the binding (or absence of binding) of a triangular substructure to a target (in a computational model based on the assay results) provides spatially and chemically specific information about a configuration of binding points in the target.

Thus, spatially and chemically specific information (e.g., 3-point pharmacophores in a target) may be obtained from assay results describing whether various gauges bind or not, in combination with knowledge of the structure of the gauges.

Furthermore, as discussed in the instant application, additional information may be obtained when a plurality of triangular substructures have been characterized as matching a target.

For example, a spatially and chemically specific 3-dimensional configuration of 4 or more binding points may be identified by constructing such a configuration from triangular substructures which match the target (see for example, pages 40-45, Sections 6.2-6.4, of the instant application).

Applicant submits that the above example indicates that spatially and chemically specific information can be obtained from simple *in vitro* assay results for gauges (e.g., measuring binding of gauges), in combination with knowledge of the structure of the gauges, using a model comprising triangular geometric substructures, as recited in claim 1. Applicant wishes to note that various embodiments of the claimed method are described in more detail in the specification.

Applicant believes to have overcome the Examiner's rejections in this respect.

In re Application of: Dror OFER  
Serial No.: 10/523,131  
Filed: January 21, 2005  
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.  
Group Art Unit: 1631  
Attorney Docket: **35898**  
Confirmation No.: 1264

In view of the above amendments and remarks, it is respectfully submitted that claims 1-4, 6-25, 29-57, 102, 103, 157-159 and 161-163 are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

**/Jason H. Rosenblum/**

Jason H. Rosenblum  
Registration No. 56,437  
Telephone: 718.246.8482

Date: January 3, 2011

**Enclosures:**

- Petition for Extension (One Month)